Abstracts

750 A PHASE 1 TRIAL OF CUE-102, A NOVEL WT1-PHLA-IL2-FC FUSION PROTEIN IN HLA-A*0201 POSITIVE PATIENTS WITH WT1-POSITIVE RECURRENT/METASTATIC CANCERS

Background Immuno-STATs are modular fusion proteins designed for the selective activation of tumor antigen specific CD8+ T cells. CUE-102, the second Immuno-STAT in clinical trials, is composed of a human leukocyte antigen (HLA) complex, HLA-A*0201, a peptide epitope derived from the Wilms Tumor 1 (WT1) protein, and 4 molecules of reduced affinity human interleukin-2 (IL-2), and is designed to bind, expand, and activate WT1-specific CD8+ T cells for the treatment of WT1+ cancers. In pre-clinical studies, CUE-102 elicits selective expansion of WT1-specific cytotoxic CD8+ T cells in vitro and in vivo.

Methods CUE-102–01 is a phase 1, 2-part study evaluating the safety, tolerability, pharmacokinetics (PK), pharmacodynamics (PD), immunogenicity, and preliminary antitumor activity of CUE-102 monotherapy administered every three weeks in HLA-A*02:01 positive patients with WT1+ recurrent/metastatic colorectal, gastric/gastroesophageal Junction (GEJ), pancreatic or ovarian cancer that has progressed on conventional therapies. Trial eligibility includes HLA-A*02:01 genotype and tumor WT1 protein expression by immunohistochemistry. Part A is a dose escalation phase following 3+3 design rules with a Bayesian Logistic Regression Model (BLRM) overlay. Dose levels that exhibit an immune or tumor response may be expanded to further characterize activity and toxicity as allowed by safety rules. Part B is a dose expansion/confirmation phase in patients with colorectal cancer. Objectives include characterization of safety, PK, PD, recommended phase 2 dose (RP2D), and preliminary anti-tumor activity.

Results 12 patients have received CUE-102 monotherapy as of June 27, 2023. Doses ranging from 1 mg/kg to 4 mg/kg were determined to be safe and well-tolerated, enabling dose escalation to 8 mg/kg. Preliminary PK data support that anticipated drug exposures are observed in patients. Characterization of post-treatment expansion of WT1-reactive T cells in peripheral blood is ongoing. Stable disease of ≥ 12 weeks, as determined by RECIST 1.1, has been observed in 2 patients (1 with colorectal; 1 with gastric cancer) in the early dose cohorts, allowing for dose expansion of the 2 mg/kg cohort. Data on safety, PK, PD and preliminary anti-tumor activity from additional patients will be presented.

Conclusions CUE-102 is a novel T cell activating agent that to date demonstrates acceptable tolerability, favorable PK, and supportive preliminary PD readouts. No DLTs or drug-related SAEs have been observed in doses up to 4 mg/kg as of the data cut-off. Adverse events have been manageable and consistent with the CUE-102 mechanism of action and underlying disease. Early signs of anti-tumor activity are encouraging.

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Trial Registration Clinicaltrials.gov NCT05360680

Ethics Approval This study was approved by Ethics and Institutional Review Boards (IRBs) at all study sites. IRB names/reference numbers: UH IRB STUDY20221273, BRANY 22-06-326-01, WCG IRB1340057, Advarra MCC# 22112, JHU IRB00349569, MDACC 2022-0761. All participants gave informed consent before taking part.

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